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Harry John Wadsworth

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GE HEALTHCARE, INC.

IP DEPARTMENT 101 CARNEGIE CENTER

PRINCETON, NJ 08540-6231

EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/559,878	Applicant(s) WADSWORTH ET AL.	
	Examiner /Venkataraman Balasubramanian/	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-7 and 9-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4-7 and 9-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' response, which included amendment to claims 1, 15, 17, 19, 25 and 26, filed on 05/17/2010, are made of record. Claims 1, 4-7 and 9-28 are pending. In view of applicants' response, the 112 second paragraph rejection of claims 25 and 26 have been obviated. However, the following 112 first and second paragraph rejections made in the previous office action are maintained. In addition, the following new ground of rejection is applied to currently pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of P¹, P² and P³ groups in claim 15 renders claim 15 indefinite as there is no corresponding definition of these groups provided therein. Hence, the structural make-up of compounds embraced in claim 15 remains unknown.

In addition, it is not clear what is intended by CFP¹, OCHP¹ and CHP¹ and how the valence requirement is met with for these groups.

This rejection is same as made in the previous office action. Applicants' amendment did not overcome this rejection. Nature of P¹, P² and P³ still remains unknown and as recited appears to be monovalent. Clearly the valence requirement of the group carrying P¹, P² and P³ are not met with.

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2. Claims 15 and 17 are improper dependent claims as they fail to further limit claim 1 on which they are dependent. The amended claim 1 requires Q to be electron deficit aromatic or heteroaromatic group with one or more electron withdrawing groups. Some groups in claim 15 and species in claim 17 do not have such a limitation and the scope of these claims are broader than the claim 1. See claim 15, page 5, first three groups and page 6, first 5 groups as well as claim 17 corresponding species. They are clearly outside the scope of claim 1.

Applicants have not addressed this rejection properly. The several species in claim 15 and 17 as pointed out above are clearly do not fall under the scope of claim 1. Hence, this rejection is proper and is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7, 9-14 and 18-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Recitation of "protected version thereof" in claim 1 has no support in the specification. Support for "protected version thereof" in page 11 pointed out in the traversal is limited to Table and as whole. Recitation of "protected version thereof" in claim 1 broadens the scope of claim 1 without support in specification and is therefore new matter.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 17 includes species which are not enabled in the examples of specification.

This rejection is same as made in the previous office action. Species of claim 17 are not in the examples shown in specification. Applicants have not addressed this rejection directly. Hence, this rejection is proper for reasons stated above and is maintained.

Claims 1, 4-7 and 9-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fluoridation of diphenyliodonium salt, phenyliodonium salt bearing unsubstituted acetophenone as well as methyl and methoxy substituted acetophenone, does not reasonably provide enablement for any or all iodonium salt and fluoridation any or all aromatic or heteroaromatic compounds generically embraced in claim 1 and compounds with diverse structure embraced in claims 15 and 17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

In evaluating the enablement question, following factors are considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include:
1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack

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thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to production of aromatic or heteroaromatic fluorine labeled compound by fluoridation of iodonium salt with fluoride in a solvent comprising water. Specification is not adequately enabled for fluoridation of any or all iodonium salt and fluoridation of any or all aromatic or heteroaromatic compounds including those with various reactive functional groups which may be susceptible to the reactions embraced in the process generically embraced in claim 1 and compounds with diverse structure embraced in claims 15 and 17.

Instant claims recites fluoridation of any iodonium salt but the nucleophilic displacement can occur on both sides of the iodonium salts and if these groups are not aromatic and heteroaromatic, the reaction will not lead to desired product namely fluorinated aryl or heteroaryl. There is no showing in the specification how to one make fluorinated aryl or heteroaryl with such starting materials. Even if one of the group is aryl or heteroaryl there is no guarantee that the reaction would occur to yield fluorinated aryl or heteroaryl. Specification is silent about how to perform the reaction in such cases and arrive at the desired product. In addition, as recited the starting iodonium salt is permitted to be any compound thereby permitting variously substituted iodonium salts. Such a recitation would not exclude reactive groups which may also participate in the said fluoridation reaction. Specification offers no teachings or suggestion as to how to

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perform the process of claim 1 in presence of these reactive groups. Specification has no teaching or suggestion as how to make the starting material for the said fluoridation with any substituents including reactive groups. The same is true for the compounds shown in claim 15 and claim 17. There is no teaching of how fluoridation of such compounds is achieved and what starting material is used. Specification offers no teachings or suggestion as to how to perform the process of claim 1 for making these compounds. Note US 2006/0292060 (apparently instant applicants) states:

The use of this reaction in the radiofluoridation of iodonium salts has been reported by Pike et al [1995 J Chem Soc Chem Comm pp2215-16] although with variable radiochemical yield (ROY). The reason for the variability in RCY was not understood. Subsequent reports from the same group [Shah et al 1998 J Chem Soc (Perkin Trans 1) 25 pp2043-6 and Martin-Santamaria et al 2000 Chem Comm pp649-50] do not offer any further explanation for the variable RCY: More recently, Wust et al [2001 J Labelled Compd Radiopharm 44 ps12-3] reported that the reaction of phenyliodonium tosylate with [^{18}F] potassium fluoride (in the presence of Kryptofix TM) yielded a very low amount of the desired [^{18}F] corticosteroid. Furthermore, the present applicants have found that radiofluoridation of iodonium salts according to the methods described above produces highly variable RCY (5% to 40%) of the desired [^{18}F] aryl fluoride product. Such lack of reproducibility makes the use of iodonium salts for the synthesis of [^{18}F] aryl fluorides problematic.

Thus, it clear that the fluoridation process is a specialized art with certain degree of unpredictability. A process which viable for one starting material need not do so for

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others. Hence, specification should teach or suggest how to make such compounds with varying structural cores and substituents. Presence of reactive groups would be chemically incompatible the process of fluoridation embraced in the instant claims. Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

2. The predictability or lack thereof in the art:

Hence the process as applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s).

4. The amount of direction or guidance present: Examples illustrated in the experimental section or written description offer no guidance or teachings as to how perform the process of claim 1 when reactive substituents or chemically incompatible substituents are present in the starting material.

5. The presence or absence of working examples:

Although examples in specification show the fluoridation process, they are limited to compound with no reactive functionality. There are no representative examples showing the viability of the process for plurality of reactive substituents embraced in the instant claims.

6. The breadth of the claims:

Specification has no support, as noted above, for all compounds generically embraced in the claim language would lead to desired compound of formula I with said reactive groups and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward the halogenating agent embraced in the process claim.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula I embraced in the instant claims.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of reactant- reagent interactions in general, and the lack of working examples regarding the viability of the claimed compounds and processes of making embraced in the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or

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use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

This rejection is same as made in the previous office action. Applicants' traversal is not persuasive for reasons of record. As recited, applicants' claims are reach through claims. Based on the fluoridation of diphenyliodonium salt, phenyliodonium salt bearing unsubstituted acetophenone as well as methyl and methoxy substituted acetophenone, instant claims reach through for fluoridation of any or all iodonium salt and fluoridation any or all aromatic or heteroaromatic compounds even those that are not are electron deficient. See claim 15 and 17 as well as claim 19 which includes any iodonium salt. See also claim 25 and 26 which embraced iodonium salts of undefined formulae

Applicants have argued that instant Q is now defined as electron deficient aryl or hereroaryl. Contrary to applicants' urging, the not all choices of Q include electron deficient groups. For example, some groups in claim 15 and species in claim 17 do not have such a limitation and the scope of these claims are broader than the claim 1. See claim 15, page 5, first three groups and page 6, first 5 groups as well as claim 17 corresponding species. Note also the choice of R^1 - R^5 includes such groups and therefore there the nucleophilic attack can give both products, Q-F and Aryl-F. Again claim 19 , 25 and 26 include any iodonium salts.

As noted above, the radio fluorination is specialized art and applicants have also provided Welch as evidence to that. The examples shown in the specification is limited

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to simple compounds and not for the diverse compounds claimed generically and more specifically in claims 15 and 17. Hence, these examples cannot be deemed as objective enablement as the species and genus recited are various largely and each required a distinct process for making the intermediates and there is no guarantee that fluoridation would work on all of them. Furthermore, the radiofluorination is specialized art and required guidance. A radiolabelled material is distinct from unlabelled material. Hence, species claimed in claims 15 and 17 require support in specification. Applicants cannot claim species without making those species.

Applicants have argued that the process of fluoridation of iodonium salts is common general knowledge and Google shows 22 hits. The issue here whether there is scope of enablement of the fluoridation process for instant genus embraced in formula I and formula II and not enablement for isolated examples known in the prior art. In other words the rejection relates scope of enablement for process for making instant genus by the process embraced in instant invention.

Applicants have not shown that instant genus of compounds were already known and were made by fluoridation of iodonium salts and that instant process and prior art process differs only in solvent composition for the fluoridation. If such is the case, applicants should provide those references which disclose all the compounds of instant genus as a support for scope of enablement to obviate this rejection. For want of such references, this rejection is proper.

Applicants have also argued that radiofluoridation is well known and that instant process differs in having in the reaction comprising water. The issue here is not whether

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radiofluoridation is known. The scope enablement issue is related the huge genus of compounds for which radiofluoridation and fluoridation is not known with starting materials embraced in claim 1. The examples shown in specification is limited few compounds and it cannot be deemed as objective enablement for the whole structurally varied compounds of the genus. Applicants asserted that presence of water alters the reaction as compared to prior art and is clear that the process is susceptible any variations in parameters. One trained in the art has to unduly extensive experimentation and even then there is no guarantee that the process is viable with various structural variations embraced in compound formula I and formula II.

Hence, this rejection is proper and is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624